

1. A method for enhancing bone repair in a mammal, comprising the administration of an amount effective for enhancing bone repair in the mammal of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R¹-R⁸ in the sequence of general formula I

$$R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}-R^{8}$$

in which R¹ and R² together form a group of formula

$$X-R^A-R^B$$
-,

wherein X is H or a one to three peptide group, or is absent,

R^A is suitably selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

 R^4 is selected from the group consisting of Tyr, $Tyr(PO_3)_2$, Thr, Ala, Ser, homoSer and azaTyr,

R⁵ is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly;

R⁶ is His, Arg or 6-NH₂-Phe;

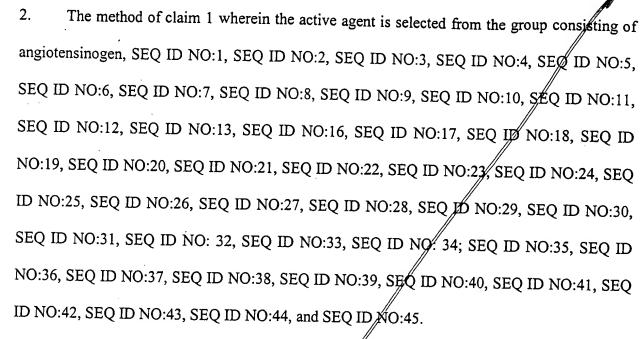
R is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent.

10

15

20



- 3. The method of claim 1 further comprising administration of an amount effective for enhancing bone repair in the mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-6, bone morphogenic protein-7, transforming growth factor-beta, insufir-like growth factor, and parathyroid hormone.
- 4. An improved method for bone and prosthesis implantation in a mammal, comprising the administration of an amount effective for enhancing bone and prosthesis implantation in the mammal of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R¹-R⁸ in the sequence of general formula I

$$R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}-R^{8}$$

in which R1 and R2 together form a group of formula

$$X-R^A-R^B$$
-,

wherein X is H or a one to three peptide group, or is absent,

R^A is suitably selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

10

15

20

R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg, and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

R⁴ is selected from the group consisting of Tyr, Tyr(PØ₃)₂, Thr, Ala, Ser, homoSer and azaTyr;

R⁵ is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly;

R⁶ is His, Arg or 6-NH₂-Phe;

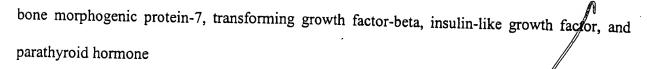
R⁷ is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent.

- The method of claim 4 wherein the active agent is selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO:34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.
- 6. The method of claim 4 further comprising administration of an amount effective for enhancing bone and prosthesis implantation in the mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-6,

15

20



- 7. A kit for enhancing bone repair in a mammal, comprising:
- (a) administering an amount effective for enhancing bone repair in the mammal of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R¹-R⁸ in the sequence of general formula I

$$R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}-R^{8}$$

in which R1 and R2 together form a group of formula

$$X-R^A-R^B$$
-,

wherein X is H or a one to three peptide group, or is absent,

R^A is suitably selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

R⁴ is selected from the group consisting of Tyr, Tyr(PO₃)₂, Thr, Ala, Ser, homoSer and azaTyr;

R⁵/is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly;

R⁶ is His, Arg or 6-NH₂-Phe;

R⁷ is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent; and

15

20

- (b) instructions for using the amount effective of active agent to enhance bone repair in a mammal.
- 8. The kit of claim 7 wherein the active agent is selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO: 34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.
 - 9. The kit of claim 7 further composing an amount effective for enhancing bone repair in the mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-6, bone morphogenic protein-7, transforming growth factor-beta, insulin-like growth factor, and parathyroid hormone.
 - 10. The kit of claim 7 further comprising a means for delivery of the active agent.
 - 11. A kit for improved bone and prosthesis implantation, comprising:
 - (a) an amount effective to enhance bone and prosthesis implantation in a mammal of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R¹-R⁸ in the sequence of general formula I

$$R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}-R^{8}$$

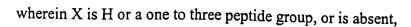
in which R1 and R2 together form a group of formula

$$X-R^A-R^B$$
-,

10

15

20



R^A is suitably selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

R⁴ is selected from the group consisting of Tyr, Tyr(PO₃)₂, Thr, Ala, Ser, homoSer and azaTyr;

R⁵ is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly;

R⁶ is His, Arg or 6-NH₂-Phe

R⁷ is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent; and

- (b) instructions for using the amount effective of active agent to enhance bone and prosthesis implantation in a mammal.
- The kit of claim 11 wherein the active agent is selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO:35, SEQ I

NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.

- The kit of claim 11 further comprising an amount effective for enhancing bone repair in the mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-6, bone morphogenic protein-7, transforming growth factor-beta, insulin-like growth factor, and parathyroid hormone.
- 14. The kit of claim 11 further comprising a means for delivery of the active agent.
- 15. A method for enhancing cartilage repair in a mammal, comprising the administration of an amount effective to enhance cartilage repair to the mammal of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R¹-R⁸ in the sequence of general formula I

$$R^{1}-R^{2}-R^{3}-R^{4}-R^{6}-R^{7}-R^{8}$$

in which R1 and R2 together form a group of formula

$$X-R^A/R^B$$

wherein X is H or a one to three peptide group, or is absent,

R^A is suitably selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

R^B/is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

 R^4 is selected from the group consisting of Tyr, $Tyr(PO_3)_2$, Thr, Ala, Ser, homoSer and azaTyr.

20

10

15

20

R⁵ is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly; R⁶ is His, Arg or 6-NH₂-Phe;

R⁷ is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent.

- 16. The method of claim 15 wherein the active agent is selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.
- 17. A kit for enhancing cartilage repair in a mammal, comprising:
 - (a) an amount effective to enhance cartilage repair in a mammal of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R¹-R⁸ in the sequence of general formula I

$$R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}-R^{8}$$

in which R1 and R2 together form a group of formula

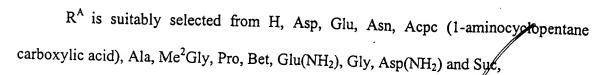
 $X-R^A-R^B$ -,

wherein X is H or a one to three peptide group, or is absent,

10

15

20



R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

 R^4 is selected from the group consisting of Tyr, $Tyr(PO_3)_2$, Thr, Ala, Ser, homoSer and azaTyr;

R⁵ is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly;

R⁶ is His, Arg or 6-NH₂-Phe;

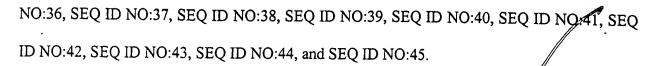
R⁷ is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent; and

- (b) instructions for using the amount effective of active agent for enhancing cartilage repair in a mammal.
- The kit of claim 17 wherein the active agent is selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO:35, SEQ I

10

15



19. An improved method for attachment and fixation of cartilage implants to bone or other tissue in a mammal, comprising the administration of an amount effective for attaching and fixing cartilage implants to bone or other tissue in a mammal of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R¹-R⁸ in the sequence of general formula I

$$R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}-R^{8}$$

in which R1 and R2 together form a group of formula

$$X-R^A-R^B$$
-,

wherein X is H or a one to three peptide group, or is absent,

R^A is suitably selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

R⁴ is selected from the group consisting of Tyr, Tyr(PO₃)₂, Thr, Ala, Ser, homoSer and azaTyr;

R⁵ is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly;

R⁶ is His, Arg or 6-NH₂-Phe;

R⁷ is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent.

- 20. The method of claim 19 wherein the active agent is selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17 SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO:34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.
- 21. A kit for improved attachment and exation of cartilage implants to bone or other tissue, comprising:
- (a) an amount effective to attach and fix a cartilage implant to bone or other tissue in a mammal of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R¹-R⁸ in the sequence of general formula I

$$R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}-R^{8}$$

in which R1 and R2 together form a group of formula

$$X-R^A-R^B$$
-,

20

wherein X is H or a one to three peptide group, or is absent,

R^A is suitably selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

10

15

20

R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

 R^4 is selected from the group consisting of Tyr, $Tyr(PO_3)_2$, Thr, Ala, Ser, homoSer and azaTyr;

 R^5 is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly; R^6 is His, Arg or 6-NH₂-Phe;

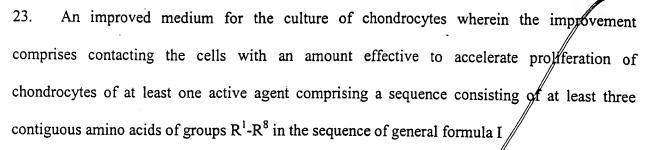
R⁷ is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent; and

- (b) instructions for using the amount effective of active agent amount effective to attach and fix a cartilage implant to bone or other tissue in a mammal.
- The kit of claim 21 wherein the active agent is selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO:34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.

15

20



$$R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}-R^{8}$$

in which R1 and R2 together form a group of formula

$$X-R^A-R^B$$
-,

wherein X is H or a one to three peptide group, or is absent,

R^A is suitably selected from H, Asp, Giu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

R⁴ is selected from the group consisting of Tyr, Tyr(PO₃)₂, Thr, Ala, Ser, homoSer and azaTyr;

R⁵ is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly; R⁶ is His, Arg or 6-NH₂-Phe;

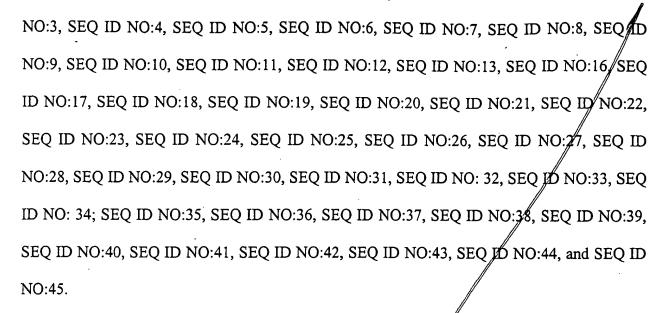
R⁷/is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent.

24. The improved chemically defined medium of claim 23 wherein the active agent is selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ÎD

10

20



- 25. A kit for the culture of chondrocytes, comprising
- (a) an amount effective to accelerate proliferation of chondrocytes of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R^1 - R^8 in the sequence of general formula I

 $R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}$

in which R1 and R2 together formula group of formula

 $X-R^A-R^B-$,

wherein X is H or a one to three peptide group, or is absent,

R^A is suitably selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³/is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

10

R⁴ is selected from the group consisting of Tyr, Tyr(PO₃)₂, Thr, Ala, Ser, homoSer and azaTyr;

R⁵ is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly; R⁶ is His, Arg or 6-NH₂-Phe;

R⁷ is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), the and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent; and

- (b) instructions for using the amount effective of active agent amount effective to accelerate proliferation of chondrocytes.
- 26. The kit of claim 25 wherein the active agent is selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO:34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.
- 27. A method for enhancing bone repair in a mammal, comprising the administration of an amount effective for enhancing bone repair in the mammal of at least one active agent of the formula

Asp-Arg-R1-R2-Ile-His-Pro-R2, wherein

R1 is selected from the group consisting of Ile, Pro, Ala, Val, Leu, and norLeu;

15

R2 is selected from Tyr and Tyr(PO₃)₂; and

R3 is Phe, or is absent.

- 28. The method of claim 27 wherein the active agent is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO: 33, SEQ ID NO:41, and SEQ ID NO: 45.
- 29. The method of claim 27 further comprising the administration of an amount effective for enhancing bone repair in the mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-6, bone morphogenic protein-7, transforming growth factor-beta, insulin-like growth factor and parathyroid hormone.
- 30. An improved method for bone and prosthesis implantation in a mammal, comprising the administration of an amount effective for enhancing bone and prosthesis implantation to the mammal of at least one active agent of the formula

Asp-Arg-R1-R2-Ile-His-Pro-R2, wherein

R1 is selected from the group consisting of Ile, Pro, Ala, Val, Leu, and norLeu;

R2 is selected from Tyr and Tyr(PO₃)₂; and

R3 is Phe, or is absent.

- 31. The method of claim 30 wherein the active agent is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO: 33, SEQ ID NO:41, and SEQ ID NO: 45.
- 32. The method of claim 30 further comprising the administration of an amount effective for enhancing borie repair in the mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-6, bone morphogenic protein-7, transforming growth factor-beta, insulin-like growth factor, and parathyroid hormone.

- 33. A kit for enhancing bone repair in a mammal, comprising:
- (a) an amount effective for enhancing bone repair in the mammal of at least one active agent of the formula

Asp-Arg-R1-R2-Ile-His-Pro-R2, wherein

R1 is selected from the group consisting of Ile, Pro, Ala, Val, Leu, and norLeu;

R2 is selected from Tyr and Tyr(PO₃)₂; and

R3 is Phe, or is absent; and

- (b) instructions for using the amount effective of active agent to enhance bone repair in a mammal.
- 10 34. The kit of claim 33 wherein the active agent is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO: 33, SEQ ID NO:41, and SEQ ID NO: 45.
 - 35. The kit of claim 33 further comprising an amount effective for enhancing bone repair in the mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-6, bone morphogenic protein-7, transforming growth factor-beta, insulin-like growth factor, and parathyroid hormone.
 - 36. The kit of claim 33/further comprising a means for delivery of the active agent.
 - 37. A kit for improved bone and prosthesis implantation, comprising:
- (a) an amount effective to enhance bone and prosthesis in a mammal of at least one active agent of the formula

Asp-Arg-R1-R2-Ile-His-Pro-R2, wherein

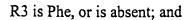
R1 is selected from the group consisting of Ile, Pro, Ala, Val, Leu, and norLeu;

R2 is selected from Tyr and Tyr(PO₃)₂; and

15

20

5



- (b) instructions for using the amount effective of active agent to enhance bone and prosthesis implantation in a mammal.
- 38. The kit of claim 37 wherein the active agent is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO: 33, SEQ ID NO:41, and SEQ ID NO: 45.
 - 39. The kit of claim 37 further comprising an amount effective for enhancing bone repair in the mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-6, bone morphogenic protein-7, transforming growth factor-beta, insulin-like growth factor, and parathyroid hormone.
 - 40. The kit of claim 37 further comprising a means for delivery of the active agent.
 - 41. A method for enhancing cartilage repair in a mammal, comprising the administration of an amount effective to enhance cartilage repair to the mammal of at least one active agent of the formula

R1-R2-R3-R4-R5-His-Pro-R6, wherein

R1 is selected from the group consisting of Hydrogen, Gly, and Asp;

R2 is selected from the group consisting of Arg, Citron, or Ornithine;

R3 is selected from the group consisting of Val, Ile, Ala, Leu, and norLeu, or Pro;

R4 is selected from Tyr, Tyr(PO₃)₂, and Ala;

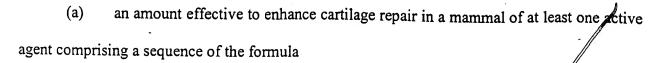
R5 is selected from the group consisting of Ile, Ala, Val, Leu, and norLeu; and R6 is Phe, Ile, or is absent.

42. / A kit for enhancing cartilage repair in a mammal, comprising:

10

15

20



R1-R2-R3-R4-R5-His-Pro-R6, wherein

R1 is selected from the group consisting of Hydrogen, Gly, and Asp;

R2 is selected from the group consisting of Arg, Citron, or Ornithing

R3 is selected from the group consisting of Val, Ile, Ala, Leu, and norLeu, or Pro;

R4 is selected from Tyr, Tyr(PO₃)₂, and Ala;

R5 is selected from the group consisting of Ile, Ala, Val, Leu, and norLeu; and

R6 is Phe, Ile, or is absent; and

(b) instructions for using the amount effective of active agent for enhancing cartilage repair in a mammal.

43. An improved method for attachment and fixation of cartilage implants to bone or other tissue in a mammal, comprising the administration of an amount effective for attaching and fixing cartilage implants to bone or other issue in a mammal of at least one active agent of the formula

R1-R2-R3-R4-R5-His-Pro-R6, wherein

R1 is selected from the group consisting of Hydrogen, Gly, and Asp;

R2 is selected from the group consisting of Arg, Citron, or Ornithine;

R3 is selected from the group consisting of Val, Ile, Ala, Leu, and norLeu, or Pro;

R4 is selected from Tyr, Tyr(PO₃)₂, and Ala;

R5 is selected from the group consisting of Ile, Ala, Val, Leu, and norLeu; and R6 is Phe, Ile, or is absent.

10

15

20

- 44. A kit for improved attachment and fixation of cartilage implants to bone or other tissue, comprising:
- (a) an amount effective to attach and fix a cartilage implant to bone or other tissue in a mammal of at least one active agent comprising a sequence of the formula
 - R1-R2-R3-R4-R5-His-Pro-R6, wherein

R1 is selected from the group consisting of Hydrogen, Gly, and Asp;

R2 is selected from the group consisting of Arg, Citron, or Ornithine;

R3 is selected from the group consisting of Val, Ile, Ala, Ley, and norLeu, or Pro;

R4 is selected from Tyr, Tyr(PO₃)₂, and Ala;

R5 is selected from the group consisting of Ile, Ala, Nal, Leu, and norLeu; and

R6 is Phe, Ile, or is absent; and

- (b) instructions for using the amount effective of active agent amount effective to attach and fix a cartilage implant to bone or other issue in a mammal.
- 45. An improved medium for the culture of chondrocytes wherein the improvement comprises contacting the cells with an amount effective to accelerate proliferation of chondrocytes of at least one active agent comprising a sequence of the formula

R1-R2-R3-R4-R5-His-Pro-R6, wherein

R1 is selected from the group consisting of Hydrogen, Gly, and Asp;

R2 is selected from the group consisting of Arg, Citron, or Ornithine;

R3 is selected from the group consisting of Val, Ile, Ala, Leu, and norLeu, or Pro;

R4 is selected from Tyr, Tyr(PO₃)₂, and Ala;

Rs is selected from the group consisting of Ile, Ala, Val, Leu, and norLeu; and

R6 is Phe, Ile, or is absent.

15

20

- 46. A kit for the culture of chondrocytes, comprising
- (a) an amount effective to accelerate proliferation of chondrocytes of at least one active agent comprising a sequence of the formula

R1-R2-R3-R4-R5-His-Pro-R6, wherein

R1 is selected from the group consisting of Hydrogen, Gly, and Asp;

R2 is selected from the group consisting of Arg, Citron, or Ornithine;

R3 is selected from the group consisting of Val, Ile, Ala/Leu, and norLeu, or Pro;

R4 is selected from Tyr, Tyr(PO₃)₂, and Ala;

R5 is selected from the group consisting of Ile, Ala, Val, Leu, and norLeu; and

R6 is Phe, Ile, or is absent; and

- (b) instructions for using the amount effective of active agent amount effective to accelerate proliferation of chondrocytes.
- 47. A pharmaceutical composition comprising
- (a) an amount effective to enhance bone repair or bone and prosthesis implantation in a mammal of at least one active agent comprising a sequence of the formula

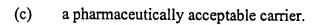
Asp-Arg-R1-R2-Ile-His-Pro-R2, wherein

R1 is selected from the group consisting of Ile, Pro, Ala, Val, Leu, and norLeu;

R2 is selected from Tyr and Tyr(PO₃)₂; and

R3 is Phe, or is absent; and

(b) an amount effective to enhance bone repair or bone and prosthesis implantation in a mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-6, bone morphogenic protein-7, transforming growth factor-beta, insulin-like growth factor, and parathyroid hormone; and



- 48. A pharmaceutical composition comprising
- (a) an amount effective to enhance bone repair or bone and prosthesis implantation in a mammal of at least one active agent comprising a sequence consisting of at least three contiguous amino acids of groups R¹-R⁸ in the sequence of general formula I

$$R^{1}-R^{2}-R^{3}-R^{4}-R^{5}-R^{6}-R^{7}-R^{8}$$

in which R1 and R2 together form a group of formula

$$X-R^A-R^B$$
-,

wherein X is H or a one to three peptide group, or is absent,

R^A is suitably selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me²Gly, Pro, Bet, Glu(NH₂), Gly, Asp(NH₂) and Suc,

R^B is suitably selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R³ is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

R⁴ is selected from the group consisting of Tyr, Tyr(PO₃)₂, Thr, Ala, Ser, homoSer and azaTyr;

R⁵ is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly;

R⁶ is His, Arg or 6-NH₂-Phe;

R//is Pro or Ala; and

R⁸ is selected from the group consisting of Phe, Phe(Br), Ile and Tyr, excluding sequences including R⁴ as a terminal Tyr group, or is absent;

10

5

15

- (b) an amount effective to enhance bone repair or bone and prosthesis implantation in a mammal of at least one compound selected from bone morphogenic protein-2, bone morphogenic protein-4, bone morphogenic protein-5 bone morphogenic protein-7, transforming growth factor-beta, insulin-like growth factor, and parathyroid hormone; and
 - (c) a pharmaceutically acceptable carrier.

